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DATE: Monday, March 27, 2006

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		<i>DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR</i>	
<input type="checkbox"/>	L1	moraxell\$.ti,ab,clm.	777
<input type="checkbox"/>	L2	toxin or cytotoxin or cytolysin or cyto-toxin or cyto-lysin or cytolytic or cyto-lytic or corneotoxin or corneo-toxin or corneotoxic or hemolytic or hemolysis or hemo-lytic or hemolysin or hemo-lysin	77159
<input type="checkbox"/>	L3	L2 and l1	160
<input type="checkbox"/>	L4	L2ti,ab,clm. and l1	0
<input type="checkbox"/>	L5	L2.ti,ab,clm. and l1	63
<input type="checkbox"/>	L6	(george.in. or angelos!.in. or hess.in.) and l1	10
<input type="checkbox"/>	L7	l6 and tifton\$	1

END OF SEARCH HISTORY

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-
- ☐ 51. [WO 200257281A](#). New aminoglycoside compounds used for treating bacterial infections caused by bacterium including *Escherichia coli*, *Pseudomonas* spp., *Proteus* spp., *Bacteroids* spp. and *Haemophilus influenzae*. HADDAD, J, et al. A61K031/704 C07H000/00 C07H015/224.
-
- ☐ 52. [US20020115621A](#). New macrolide compound useful as antibacterial and antiprotozoal agent for mammals. CHEN, Y, et al. A61K031/70 A61K031/7048 A61K031/7052 A61P031/04 A61P033/02 A61P043/00 C07H017/08.
-
- ☐ 53. [WO 200192280A](#). New hygromycin derivatives used for treating bacterial and protozoal infections e.g. pneumonia, otitis media, sinusitis or bronchitis. HAYWARD, M M, et al. A61K031/341 A61K031/357 A61K031/36 A61K031/443 A61K031/496 A61K031/655 A61K031/70 A61K031/7004 A61K031/7034 A61K031/7048 A61P031/04 A61P031/10 A61P033/02 C07D317/66 C07D405/02 C07D405/14 C07D407/12 C07H000/00 C07H015/203.
-
- ☐ 54. [WO 200116172A](#). Novel *Moraxella* bovis antigen useful in compositions for raising immune response in an animal, has protease, lipase or hemolysin activity. FAM, J, et al. A61K038/48 A61K039/095 C07K014/22 C07K016/12 C12N015/31.
-
- ☐ 55. [US20020061281A](#). Aerosol composition for treatment of sinusitis comprising one or more anti-infective, anti-inflammatory and/or anti-mucolytic agents e.g. cefuroxime. HALE, M A, et al. A61K009/00 A61K009/12 A61K009/14 A61K047/02 A61K047/34 A61L000/00 A61L009/04 A61P011/02 A61P031/00.
-
- ☐ 56. [WO 200064457A](#). Composition having genetically modified live oral commensal bacteria which express immunogenic fragments of mucosal pathogens, used as oral vaccines to treat host against *Bordetella pertussis*, poliovirus infection. HALPERIN, S A, et al. A61K035/00 A61K039/00 A61K048/00 C12N001/20.
-
- ☐ 57. [WO 200034297A](#). New carbamate and carbazate ketolide derivatives, useful for treatment of bacterial and protozoal infections and related disorders e.g. pneumonia, otitis media, bronchitis, rheumatic fever, glomerulonephritis and ulcers. KANEKO, T, et al. A61K031/70 A61P031/04 A61P033/02 C07D421/00 C07H017/08.
-
- ☐ 58. [US 6365574B](#). Non-hygroscopic azithromycin ethanolate compounds useful for treating microbial infections and a method for their preparation. ARONHIME, J, et al. A01N043/04 A61K000/00 A61K031/70 A61K031/7048 A61K031/7052 A61P031/04 C07H001/00 C07H017/00 C07H017/02 C07H017/08.
-
- ☐ 59. [US20020040007A](#). New macrolide derivatives, useful for treatment of e.g. bacterial and protozoal infections and related disorders e.g. pneumonia and rheumatic fever, and cancer. KANEKO, T, et al. A61K000/00 A61K031/70 A61K031/7048 A61P001/00 A61P001/02 A61P001/04 A61P009/00 A61P009/10 A61P011/00 A61P011/14 A61P013/02 A61P013/12 A61P015/00 A61P027/02 A61P027/16 A61P031/04 A61P033/00 A61P033/02 A61P035/00 C07H017/00 C07H017/08.
-
- ☐ 60. [WO 200018434A](#). New mutant cholera holotoxin having a point mutation at amino acid position 29 of the A subunit useful as an adjuvant in an antigenic composition to enhance the immune

response in a vertebrate host to a selected antigen from a pathogen. ELDRIDGE, J H, et al. A61K039/00 A61K039/002 A61K039/02 A61K039/095 A61K039/102 A61K039/106 A61K039/12 A61K039/15 A61K039/155 A61K039/245 A61K039/39 A61P037/04 C07K014/14 C07K014/22 C07K014/28 C07K014/285 C07K014:28 C12N001/15 C12N001/19 C12N001/21 C12N005/10 C12N015/09 C12N015/63 C12P021/02.

☐ 61. US 6342497B. New 2"-deoxy-hygromycin A derivatives used for treating bacterial and protozoal infections. LINDE, R G. A61K031/36 A61K031/4409 A61K031/70 A61K031/7048 A61P031/04 C07D000/00 C07D317/46 C07D405/10 C07D405/14 C07H015/26.

☐ 62. US 6313100B. New hygromycin A derivatives used for treating bacterial and protozoal infections. BRIGHTY, K E, et al. A61K031/70 A61K031/7048 A61K039/02 A61P031/00 A61P031/04 A61P033/02 C07D000/00 C07H015/00 C07H015/203 C07H015/26 C12P001/04 C12P019/00 C12P019/44 C12P019/46 C12P019/54.

☐ 63. WO 9007525A. Keratoconjunctivitis cytotoxin from Moraxella bovis - toxic to bovine peripheral blood neutrophils but lacks haemolytic activity. GEORGE, L W, et al. A61K037/48 A61K039/02 C07K015/00.

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Term	Documents
(1 AND (2.TI,AB,CLM.)).PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD.	63
(L2.TI,AB,CLM. AND L1).PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD.	63

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-
- ☐ 56. [WO 200064457A](#). Composition having genetically modified live oral commensal bacteria which express immunogenic fragments of mucosal pathogens, used as oral vaccines to treat host against *Bordetella pertussis*, poliovirus infection. HALPERIN, S A, et al. A61K035/00 A61K039/00 A61K048/00 C12N001/20.
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-
- ☐ 59. [US20020040007A](#). New macrolide derivatives, useful for treatment of e.g. bacterial and protozoal infections and related disorders e.g. pneumonia and rheumatic fever, and cancer. KANEKO, T, et al. A61K000/00 A61K031/70 A61K031/7048 A61P001/00 A61P001/02 A61P001/04 A61P009/00 A61P009/10 A61P011/00 A61P011/14 A61P013/02 A61P013/12 A61P015/00 A61P027/02 A61P027/16 A61P031/04 A61P033/00 A61P033/02 A61P035/00 C07H017/00 C07H017/08.
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Term	Documents
(1 AND (2.TI,AB,CLM.)).PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD.	63
(L2.TI,AB,CLM. AND L1).PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD.	63

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☐ tr Q43892 _ACTAC Leukotoxin [LKTA] [Actinobacillus actinomycetemc
☐ tr Q46716 _ECO57 Hemolysin A (Hemolysin toxin protein) [hlyA] [Es
☐ tr P71223 _ECOLI EHEC-hemolysin [EHEC-hlyA] [Escherichia coli]
☐ sp P55129 RTX12_ACTPL RTX-I toxin determinant A from serotypes 5.
☐ sp P55128 RTX11_ACTPL RTX-I toxin determinant A from serotypes 1.
☐ tr Q47461 _ECOLI EHEC-hlyA protein [EHEC-hlyA] [Escherichia coli]
☐ tr Q47262 _ECOLI Hemolysin [EHEC-hlyA] [Escherichia coli]
☐ sp P16462 LKTA_ACTAC Leukotoxin (Lkt) [lktA] [Actinobacillus act.
☐ tr Q79D75 _ECOLI HlyA (Fragment) [hlyA] [Escherichia coli]
☐ tr Q5MK37 _9PAST Leukotoxin A (Fragment) [lktA] [Pasteurellaceae
☐ tr Q5MK35 _9PAST Leukotoxin A (Fragment) [lktA] [Pasteurellaceae
☐ tr Q5MK32 _9PAST Leukotoxin A (Fragment) [lktA] [Pasteurellaceae
☐ tr Q5MK34 _9PAST Leukotoxin A (Fragment) [lktA] [Pasteurellaceae
☐ tr Q5MK29 _9PAST Leukotoxin A (Fragment) [lktA] [Pasteurellaceae
☐ tr Q5MK27 _9PAST Leukotoxin A (Fragment) [lktA] [Pasteurellaceae
☐ tr Q5MK36 _9PAST Leukotoxin A (Fragment) [lktA] [Pasteurellaceae
☐ tr Q5MK40 _9PAST Leukotoxin A (Fragment) [lktA] [Pasteurellaceae
☐ tr Q5MK38 _9PAST Leukotoxin A (Fragment) [lktA] [Pasteurellaceae
☐ tr Q5MK39 _9PAST Leukotoxin A (Fragment) [lktA] [Pasteurellaceae
☐ tr Q5MK41 _9PAST Leukotoxin A (Fragment) [lktA] [Pasteurellaceae
☐ tr Q5MK33 _9PAST Leukotoxin A (Fragment) [lktA] [Pasteurellaceae
☐ tr Q5MK26 _9PAST Leukotoxin A (Fragment) [lktA] [Pasteurellaceae
☐ tr Q5MK28 _9PAST Leukotoxin A (Fragment) [lktA] [Pasteurellaceae
☐ tr Q5MK30 _9PAST Leukotoxin A (Fragment) [lktA] [Pasteurellaceae
☐ tr Q5MK25 _9PAST Leukotoxin A (Fragment) [lktA] [Pasteurellaceae
☐ sp Q57506 CYAA_BORBR Bifunctional hemolysin-adenylate cyclase pr.
☐ sp P15318 CYAA_BORPE Bifunctional hemolysin-adenylate cyclase pr.
☐ tr Q7W1N2 _BORPA Bifunctional hemolysin-adenylate cyclase (EC 4.6
☐ tr Q9L469 _BORPA Bifunctional hemolysin-adenylate cyclase (EC 4.6
☐ tr Q3SAJ8 _9BORD Adenylate cyclase toxin [cyaA] [Bordetella hinzi
☐ tr Q2PUJ2 _MANGL Leukotoxin structural protein (Fragment) [lktA]
☐ tr Q2PUJ8 _PASHA Leukotoxin structural protein (Fragment) [lktA]
☐ tr Q2PUJ6 _MANGL Leukotoxin structural protein (Fragment) [lktA]
☐ tr Q2PUH9 _9PAST Leukotoxin structural protein (Fragment) [lktA]
☐ tr Q2PUI3 _9PAST Leukotoxin structural protein (Fragment) [lktA]
☐ tr Q2PUJ7 _PASHA Leukotoxin structural protein (Fragment) [lktA]
☐ tr Q2PUI8 _MANGL Leukotoxin structural protein (Fragment) [lktA]
☐ tr Q2PUI5 _9PAST Leukotoxin structural protein (Fragment) [lktA]
☐ tr Q5MK31 _9PAST Leukotoxin A (Fragment) [lktA] [Pasteurellaceae
☐ tr Q2PUI7 _9PAST Leukotoxin structural protein (Fragment) [lktA]
☐ tr Q2PUI6 _9PAST Leukotoxin structural protein (Fragment) [lktA]
☐ tr Q2PUH6 _9PAST Leukotoxin structural protein (Fragment) [lktA]

- ☐ tr Q2PUH5 _9PAST Leukotoxin structural protein (Fragment) [lktA]
- ☐ tr Q2PUI1 _9PAST Leukotoxin structural protein (Fragment) [lktA]
- ☐ tr Q6RKA4 _ECOLI HlyA (Fragment) [Escherichia coli]
- ☐ tr O68404 _ECOLI Alpha hemolysin (Fragment) [hlyA] [Escherichia c
- ☐ tr O70070 _ECOLI Alpha hemolysin (Fragment) [hlyA] [Escherichia c
- ☐ tr O68403 _ECOLI Alpha hemolysin (Fragment) [hlyA] [Escherichia c
- ☐ tr Q8VQ26 _ECOLI HlyA (Fragment) [Escherichia coli]
- ☐ tr Q8VQ38 _9ENTR HlyA (Fragment) [hlyA] [Citrobacter rodentium]
- ☐ tr Q83WM0 _ECO57 Hemolysin (Fragment) [hlyA] [Escherichia coli O1
- ☐ tr Q937W0 _BORBR Adenylate cyclase hemolysin (Fragment) [cyaA] [B
- ☐ tr Q937V6 _BORBR Adenylate cyclase hemolysin (Fragment) [cyaA] [B
- ☐ tr Q937W1 _BORBR Adenylate cyclase hemolysin (Fragment) [cyaA] [B
- ☐ tr Q937V9 _BORBR Adenylate cyclase hemolysin (Fragment) [cyaA] [B
- ☐ tr Q937V8 _BORBR Adenylate cyclase hemolysin (Fragment) [cyaA] [B

Graphical overview of the alignments

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to resubmit your query after masking regions matching PROSITE profiles or Pfam HMMs

([?](#) Help) (use ScanProsite for more details about PROSITE matches)

Profile hits

Pfam hits





Alignments

tr	Q93GI2	RTX toxin [mbxA] [Moraxella bovis]	92%
	Q93GI2 MORBO		align

Score = 1612 bits (4175), Expect = 0.0
Identities = 850/927 (91%), Positives = 850/927 (91%)

Query: 1	MSNINVIKSNIQAGLNSTKSGLKNLYLAIPKDYDPQKGGTLNDFIKAADELGIARL MSNINVIKSNIQAGLNSTKSGLKNLYLAIPKDYDPQKGGTLNDFIKAADELGIARL
Sbjct: 1	MSNINVIKSNIQAGLNSTKSGLKNLYLAIPKDYDPQKGGTLNDFIKAADELGIARL
Query: 61	NHTETAKKSVDTVNQFLSLTQTGIAISATKLEKFLQKHSTNKLAKGLDSVENIDRK NHTETAKKSVDTVNQFLSLTQTGIAISATKLEKFLQKHSTNKLAKGLDSVENIDRK
Sbjct: 61	NHTETAKKSVDTVNQFLSLTQTGIAISATKLEKFLQKHSTNKLAKGLDSVENIDRK
Query: 121	SNVLSTLSSFLGTALAGIELDSLIIKKGDAAPDALAKASIDLINEIIGNLSQSTQTI SNVLSTLSSFLGTALAGIELDSLIIKKGDAAPDALAKASIDLINEIIGNLSQSTQTI
Sbjct: 121	SNVLSTLSSFLGTALAGIELDSLIIKKGDAAPDALAKASIDLINEIIGNLSQSTQTI
Query: 181	SQLAKLGSTISQAKGFSNIGNKLQNLNFSKTNLGLEIITGLLSGISAGFALADKNA SQLAKLGSTISQAKGFSNIGNKLQNLNFSKTNLGLEIITGLLSGISAGFALADKNA
Sbjct: 181	SQLAKLGSTISQAKGFSNIGNKLQNLNFSKTNLGLEIITGLLSGISAGFALADKNA
Query: 241	KVAAGFELSNQVIGNVTKAISSYVLAQRVAAGLSTTGAVAALITSSIMLAISPLAF KVAAGFELSNQVIGNVTKAISSYVLAQRVAAGLSTTGAVAALITSSIMLAISPLAF
Sbjct: 241	KVAAGFELSNQVIGNVTKAISSYVLAQRVAAGLSTTGAVAALITSSIMLAISPLAF
Query: 301	DKFNHANALDEFAKQFRKFGYDGDHLLAEYQRGVGTIEASLTTISTALXXXXXXXXXX DKFNHANALDEFAKQFRKFGYDGDHLLAEYQRGVGTIEASLTTISTAL
Sbjct: 301	DKFNHANALDEFAKQFRKFGYDGDHLLAEYQRGVGTIEASLTTISTALGAVSAGVS
Query: 361	XXXXXXPIALLVAGVTGLISGILEASKQAMFESVANRLQGKILEWEKQNGGQNYFD PIALLVAGVTGLISGILEASKQAMFESVANRLQGKILEWEKQNGGQNYFD
Sbjct: 361	GSAVGAPIALLVAGVTGLISGILEASKQAMFESVANRLQGKILEWEKQNGGQNYFD
Query: 421	SRYAAYLANNLKFLSELNKELEAERVIAITQQRWDNNIGELAGITKLGERIKSGKA SRYAAYLANNLKFLSELNKELEAERVIAITQQRWDNNIGELAGITKLGERIKSGKA
Sbjct: 421	SRYAAYLANNLKFLSELNKELEAERVIAITQQRWDNNIGELAGITKLGERIKSGKA
Query: 481	FEDGKKVEAGSNITLDAKTGIIDISNSNGKKTQALHFTSPLLTAGTESRERLTNGK FEDGKKVEAGSNITLDAKTGIIDISNSNGKKTQALHFTSPLLTAGTESRERLTNGK
Sbjct: 481	FEDGKKVEAGSNITLDAKTGIIDISNSNGKKTQALHFTSPLLTAGTESRERLTNGK
Query: 541	NKLKFGRVKNWQVTDGEASSKLDFSQVIRVAETEGTDEIGLIVNAKAGNDDIFVG NKLKFGRVKNWQVTDGEASSKLDFSQVIRVAETEGTDEIGLIVNAKAGNDDIFVG

Sbjct: 541 NKLKFGRVKNWQVTDGEASSKLDFSKVIQ RVAETEGTDEIGLIVNAKAGNDDIFVG

Query: 601 NIDGGDGHDRVFYSKDGGFGNITVDGTSATEAGSYTVNRKVARGDIYHEVVKRQET
NIDGGDGHDRVFYSKDGGFGNITVDGTSATEAGSYTVNRKVARGDIYHEVVKRQET

Sbjct: 601 NIDGGDGHDRVFYSKDGGFGNITVDGTSATEAGSYTVNRKVARGDIYHEVVKRQET

Query: 661 RTETIQYRDYELRKVG YGYQSTDNLKSVEEVIGSQFNDVFKGSKFNDFHSHSXXXXXX
RTETIQYRDYELRKVG YGYQSTDNLKSVEEVIGSQFNDVFKGSKFNDFHSHS

Sbjct: 661 RTETIQYRDYELRKVG YGYQSTDNLKSVEEVIGSQFNDVFKGSKFNDFHSHSGEGDD

Query: 721 XXNDVYIFRKGDGNDTLYD
N NDVYIFRKGDGNDTLYD

Sbjct: 721 GAGDDRFLFGGKGNDRLSGDEGDDLLDGGSGDDVLNGGAGNDVYIFRKGDGNDTLYD

Query: 781 DKLAFADANISDIMIERTKEGIIVKRNDHSGSINIPRWYITSNLQNYQSNKTDHKKI
DKLAFADANISDIMIERTKEGIIVKRNDHSGSINIPRWYITSNLQNYQSNKTDHKKI

Sbjct: 781 DKLAFADANISDIMIERTKEGIIVKRNDHSGSINIPRWYITSNLQNYQSNKTDHKKI

Query: 841 GKDGSYITSXXXXXXXXXXXXXGTVITSQELKKLADENKSQKLSASDIASSLNKLVG
GKDGSYITS GTVITSQELKKLADENKSQKLSASDIASSLNKLVG

Sbjct: 841 GKDGSYITS DQIDKILQDKKDGTVITSQELKKLADENKSQKLSASDIASSLNKLVG

Query: 901 FGTANSVSSNALQPITQPTQGILAPSV 927
FGTANSVSSNALQPITQPTQGILAPSV

Sbjct: 901 FGTANSVSSNALQPITQPTQGILAPSV 927

sp Q9ETX2 Leukotoxin (Lkt) [lktA] [Mannheimia glucosida] 91
LKTA_MANGL a.

Score = 783 bits (2022), Expect = 0.0

Identities = 426/935 (45%), Positives = 589/935 (62%), Gaps = 25/9

Query: 2 SNINVIKSNIQAGLNSTKSG LKNLYLAIPKDY--DPQKGGTLNDFIKAADELGIAR
S +N ++ S K+G K + L IPKDY D +KG L D +KAA+ELGI

Sbjct: 21 SGLNRTGQSLAKAGQSLKTGAKKIILYIPKDYQYDTEKGNGLQDLVKAAEELGIEV

Query: 60 PNHTETAKKSVDTV NQFLSLTQTGIAISATKLEKFLQKHSTNKLAKGLDSVENIDR
N A+ S+ T+ L LT+ GI +SA +L+K LQK K+ + + S EN+ +

Sbjct: 81 GN DIAKAQTS LGTIQNVLGLTERGIVLSAPQLDKLLQK---TKVGQAIGSAENLTK

Query: 120 ASNVLSTLSSFLGTALAGIELDSL I KKGDAAPDALAKASIDLINEIIGNLSQSTQT
A VLS + S LG+ LAG++LD ++K ++ LAKA ++L N +I N++ S +T

Sbjct: 138 AKTVLSGIQSILGSVLGMDLDEALQK-NSNELTLAKAGLELTNSLIENIANSVKT

Query: 180 SSQ LAKLGSTISQAKGFSNIGNKLQNLN-FSKTNLGLEIITGLLSGISAGFALADK

Q+ +LGS + KG S++G+KL+ L+ F KT+LGL++++GLLSG +A LADK
Sbjct: 197 GDQINQLGSKLQNVKGLSSLGDKLKGLSGFDKTSGLGLDVVSGLLSGATAALVLADK

Query: 239 GKKVAAGFELSNQVIGNVTKAISSYVLAQRVAAGLSTTGAVAALITSSIMLAISPL
+KV AGFEL+NQV+GN+TKA+SSY+LAQRVAAGLS+TG VAALI S++ LAISPL
Sbjct: 257 SRKVGAGFELANQVVG NITKAVSSYILAQRVAAGLSSTGPVAALIASTVSLAISPL

Query: 299 AADKFNHANALDEFAKQFRKFGYDGDHLLAEYQRGVGTIEASLTISTALXXXXXX
ADKFNHA +L+ +A++F+K GYDGD+LLAEYQRG GTI+AS+T I+TAL
Sbjct: 317 IADKFNHAKSLESYAERFKKLG YDGDNLLAEYQRTGTIDASVTAIN TALAAIAGG

Query: 359 XXXXXXXXP IALLVAGVTGLISGILEASKQAMFESVANRLQGKILEWEKQNGGQNY
PIALLV+G+TG+IS IL+ SKQAMFE VAN++ KI+EWEEK N G+NY
Sbjct: 377 AAGSVIASPIALLVSGITGVISTILQYSKQAMFEHVANKIHNKIVEWEKNNHGKNY

Query: 419 YDSRYAAYLANNLKFLSELNKELEAERVIAITQQRWDNNIGELAGITKLGERIKSG
YD+RY A L +N+KFL LNKEL+AERVIAITQQ+WDNNIG+LAGI++LGE++ SG
Sbjct: 437 YDARYLANLQDNMKFLLNLNKELQAERVIAITQQQWDNNIGDLAGISRLGEKVLSG

Query: 479 DAFEDGKKVEAGSNITLDAKTGIIDISNSNGKKTQALHFTSPLLTAGTESRERLTN
DAFE+GK ++A + LD+ GIID+SNS KTQ + F +PLLT GTE RER+
Sbjct: 497 DAFEEGKHLKADKLVQLDSANGIIDVSNSGKAKTQHILFRTPLLTGTEHRERVQT

Query: 539 YINKLKFG RVKNWQVTDGEASSKLDFSKVIQRV-----AETEGTDEIGLIVNAK
YI KL RV +W++TDG ASS D + V+QR+ T E ++
Sbjct: 557 YITKLNINRVDSWKITDGAASSTFDLTNVVQRIGIELDNAGNVTKTKETKIVAKLG

Query: 592 DIFVGQGKMNI DGGDGHDRVFYSKDG GFGNITVDGTSATEAGSYTVNRKVARGDIY
++FVG G IDGG+G+DRV YS+ G +G +T+D T TE GSYTVNR V G
Sbjct: 617 NVFVGSGTTEIDGGEGYDRVHYSR-GNYGALTIDATKETEQGSYTVNRFVETGKAL

Query: 652 KRQETKVGKRTETIQYRDYELRKVG YGYQSTDNLKSV EEVIGSQFNDVFKGSKFND
VG R E I+YR + + GY + D LK+VEE+IG+ ND+FKGSKFND
Sbjct: 676 STHTALVGNREEKIEYR-HSNNQH HAGYYTKDTLKAVEEIIGTSHNDIFKGSKFND

Query: 712 XXXNDVYIFRK
+ +D+++ R+
Sbjct: 735 GDGVDTIDGNDGNDR LFGGKGDDIIDGGNGDDFIDGGKGN D LLHGKGDDIFVHRQ

Query: 772 DTLYDGTGNDKLAFADANISDIMIERTKEGIIVKRNDHSGSINIPRWY----ITSN
D + D GNDKL+F+D+N+ D+ E+ K +++ N + I W+
Sbjct: 795 DIITDSGNDKLSFSDSNLKD LTFEKVKHNLVI-TNSRKEKVTIQDWFREADFAKE

Query: 828 QSNKTDHKIEQLIGKDGSYITSXXXXXXXXXXXXXGTVITSQELKKLADENKSQKLS
++ K D KIE++IG++G ITS IT EL K+ D + K S
Sbjct: 854 KATK-DEKIEEIIGQNGERITS--KQVDDLI AKNGKITQDELSKVVDNYELLKHS

Query: 888 ASSLNKLVGSMALFGTANSVSSNALQPITQPTQGI 922
+SL+KL+ S + F ++N + + P + Q +
Sbjct: 910 TNSLDKLISSASAFTSSNDSRNVLVAPTSMLDQSL 944

tr Q6TB03 Leukotoxin structural protein [lktA] [Mannheimia
Q6TB03_9PAST ruminalis]

Score = 783 bits (2022), Expect = 0.0

Identities = 428/929 (46%), Positives = 588/929 (63%), Gaps = 26/9

Query: 8 KSNIQAGLNSTKSGLKNLYLAIPKD--YDPQKGGTLNDFIKADELGIARLAEFPN
+S QAG S K+G K + L IPKD YD +KG L D +KAA+ELGI EE N
Sbjct: 28 QSLAQAG-QSLKTGAKKIILYIPKDYQYDTEKGNGLQDLVKAAEELGIEVQKEEGN

Query: 66 AKKSVDTVNQFLSLTQTGIAISATKLEKFLQKHSTNKLAKGLDSVENIDRKLKAS
A+ S+ T+ L LT+ GI +SA +L+K LQK K+ + + S EN+ + A
Sbjct: 87 AQTSLGTIQNVLGLTERGIVLSAPQLDKLLQK---TKVGQAIGSTENLTGFSNAK

Query: 126 TLSSFLGTALAGIELDSLIIKKGDAAPDALAKASIDLINEIIGNLSQSTQTIEAFSS
+ S LG+ LAG++LD ++K ++ LAKA ++L N +I N++ S +T++AF
Sbjct: 144 GIQSILGSVLAGMDLDEALQK-NSNELTLAKAGLELTNSLIENIANSVKTLDAFGD

Query: 186 LGSTISQAKGFSNIGNKLQNLN-FSKTNLGLEIITGLLSGISAGFALADKNASTGK
LGS + KG S++G+KL+ L+ F KT+LGL++++GLLSG +A LADKNAST +
Sbjct: 203 LGSKLQNVKGLSSLGDKLKGLSGFDKTSGLDGVVSGLLSGATAALVLADKNASTSR

Query: 245 GFELSNQVIGNVTKAISSYVLAQRVAAGLSTTGAVAALITSSIMLAISPLAFMNAA
GFEL+NQV+GN+TKA+SSY+LAQRVAAGLS+TG VAALI S++ LAISPLAF A
Sbjct: 263 GFELANQVVG NITKAVSSYILAQRVAAGLSSTGPVAALIASTVSLAISPLAFAGIA

Query: 305 HANALDEFAKQFRKFGYDGDHLLAEYQRGVGTIEASLTTISTALXXXXXXXXXXXXX
HA +L+ +A++F+K GYDGD+LLAEYQRG GTI+AS+T I+TAL
Sbjct: 323 HAKSLESYAERFKKLGYDGDNLLAEYQRG GTGTIDASVTAIN TALAAIAGGVSA AAA

Query: 365 XXPIALLVAGVTGLISGILEASKQAMFESVANRLQGKILEWEKQNGGQNYFDKGYD
PIALLV+G+TG+IS IL+ SKQAMFE VAN++ KI+EWEEK N G+NYF+ GYD
Sbjct: 383 ASPIALLVSGITGVISTILQYSKQAMFEHVANKIHNKIVEWEKNNHGKNYFENG YD

Query: 425 AYLANNLKFLSELNKELEAERVIAITQQRWDNNIGELAGITKLGERIKSGKAYADA
A L +N+KFL LNKEL+AERVIAITQQ+WDNNIG+LAGI++LGE++ SGKAY DA
Sbjct: 443 ANLQDNMKFLLNLNKE LQAERVIAITQQQWDNNIGDLAGISRLGEKVLSGKAYVDA

Query: 485 KKVEAGSNITLDAKTGIIDISNSNGKKTQALHFTSPLLTAGTESRERLTNGKYSYI
K ++A + LD+ GIID+SNS KTQ + F +PLLT GTE RER+ GKY YI
Sbjct: 503 KHLKADKLVQLDSANGIIDVSNSGKAKTQHILFRTPLLTPGTEHRERIRIQTGKYEYI

Query: 545 FGRVKNWQVTDGEASSKLDFSKVIQRV-----AETEGTDEIGLIVNAKAGNDDI
 RV +W++TDG ASS D + V+QR+ T E ++ AG+D++
 Sbjct: 563 INRVDSWKITDGAASSTFDLTNVVQIRIGIELDNAGNVTKTKETKIVAKLGAGDDNV

Query: 598 GKMNIIDGGDGHDRVFYSKDGFGNITVDGTSATEAGSYTVNRKVARGDIYHEVVKR
 G IDGG+G+DRV YS+ G +G +T+D T TE GSYTVNR V G HEV
 Sbjct: 623 GTTEIDGGEGYDRVHYSR-GNYGALTIDATKETERGSYTVNRFVETGKALHEVTST

Query: 658 VGKRTETIQYRDYELRKVGYGQSTDNLKSVEEVIGSQFNDVFKGSKFNDIFHSXX
 VG R E I+YR + + GY + D LK+VEE+IG+ ND+FKGSKFND F+
 Sbjct: 682 VGNREEKIEYR-HSNNQHHAGYYTKDTLKAVEEIIIGTSHNDIFKGSKFNDFAFNGGD

Query: 718 XXNDVYIFRKGDGNDT
 + +D+++ R+GDGND
 Sbjct: 741 IDGNDGNDRLFGGKGDDIIDGGNGDDFIDGGKGNDDLHGGKGDDIFVHRQGDGNDI

Query: 778 TGNDKLAFADANISDIMIERTKEGIIIVKRNDHSGSINIPRWY----ITSNLQNYQS
 GNDKL+F+D+N+ D+ E+ K +++ N + I W+ + NY++
 Sbjct: 801 DGNDKLSFSDSNLKDLTFEKVKHNLVI-TNSRKEKVTIQDWFREADFAKEVPNYKA

Query: 834 HKIEQLIGKDGSIYITSXXXXXXXXXXXXXGTVITSQELKKLADENKSQKLSASDIAS
 KIE++IG++G ITS IT EL K+ D + K S ++ +
 Sbjct: 859 EKIEEIIQNGERITS--KQVDDLIAGNGKITQDELSKVVDNYELLKHS-KNVTN

Query: 894 LVGSMALFGTANSVSSNALQPITQPTQGI 922
 L+ S + F ++N + + P + Q +
 Sbjct: 916 LISSASAFTSSNDSRNVLVAPTSMLDQSL 944

sp P55118 Leukotoxin (Lkt) [lktA] [Pasteurella haemolytica
 LKA11_PASHA (Mannheimia
 haemolytica)]

Score = 778 bits (2008), Expect = 0.0

Identities = 423/935 (45%), Positives = 587/935 (62%), Gaps = 25/9

Query: 2 SNINVIKSNIQAGLNSTKSGLNLYLAIPKDY--DPQKGGTLNDFIKAADELGIAR
 S +N ++ S K+G K + L IPKDY D +KG L D +KAA+ELGI
 Sbjct: 21 SGLNRTGQSLAKAGQSLKTGAKKIILYIPKDYQYDTEKGNGLQDLVKAAEELGIEV

Query: 60 PNHTETAKKSVDTVNQFLSLTQTGIAISATKLEKFLQKHSTNKLAKGLDSVENIDR
 N A+ S+ T+ L LT+ GI +SA +L+K LQK K+ + + S EN+ +
 Sbjct: 81 GNDIAKAQTSLGTIQNVLGLTERGIVLSAPQLDKLLQK---TKVGQAIGSAENLTK

Query: 120 ASNVLSTLSSFLGTALAGIELDSLIIKKGDAAPDALAKASIDLINEIIGNLSQSTQT

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Search Results - Record(s) 1 through 15 of 15 returned.

☐ 1. Document ID: US 20040116363 A1

Using default format because multiple data bases are involved.

L12: Entry 1 of 15

File: PGPB

Jun 17, 2004

PGPUB-DOCUMENT-NUMBER: 20040116363

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040116363 A1

TITLE: Modified leukotoxin gene and protein

PUBLICATION-DATE: June 17, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Lo, Reggie Y.	Guelph		CA
Shewen, Patricia E	Guelph		CA
Lee, Raymond W	Guelph		CA
Hodgins, Doug	Milverton		CA
Strommer, Judith	Milverton		CA

US-CL-CURRENT: [514/44](#); [435/252.3](#), [435/320.1](#), [435/6](#), [435/69.1](#), [530/350](#), [536/23.7](#)

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	IMC	Draw D
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☐ 2. Document ID: US 20030065137 A1

L12: Entry 2 of 15

File: PGPB

Apr 3, 2003

DOCUMENT-IDENTIFIER: US 20030065137 A1

TITLE: Immunological methods to modulate myostatin in vertebrate subjects

CLAIMS:

46. The myostatin multimer of claim 33, wherein said multimer comprises a molecule according to the general formula (MP-X-MP)_y, wherein MP is a myostatin peptide, X is selected from the group consisting of a peptide linkage, an amino acid spacer group, a leukotoxin polypeptide and [MP].sub.n, where n is greater than or equal to 1, and y is greater than or equal to 1.

54. The myostatin immunoconjugate of claim 50, wherein the immunological carrier is a leukotoxin polypeptide.

55. The myostatin immunoconjugate of claim 51, wherein the immunological carrier is a leukotoxin polypeptide.

56. The myostatin immunoconjugate of claim 52, wherein the immunological carrier is a leukotoxin polypeptide.

57. The myostatin immunoconjugate of claim 53, wherein the immunological carrier is a leukotoxin polypeptide.

111. A recombinant vector comprising: (a) a polynucleotide according to claim 104; and (b) control elements that are operably linked to said polynucleotide whereby a coding sequence within said polynucleotide can be transcribed and translated in a host cell, and at least one of said control elements is heterologous to said coding sequence.

112. A recombinant vector comprising: (a) a polynucleotide according to claim 105; and (b) control elements that are operably linked to said polynucleotide whereby a coding sequence within said polynucleotide can be transcribed and translated in a host cell, and at least one of said control elements is heterologous to said coding sequence.

113. A recombinant vector comprising: (a) a polynucleotide according to claim 106; and (b) control elements that are operably linked to said polynucleotide whereby a coding sequence within said polynucleotide can be transcribed and translated in a host cell, and at least one of said control elements is heterologous to said coding sequence.

114. A recombinant vector comprising: (a) a polynucleotide according to claim 107; and (b) control elements that are operably linked to said polynucleotide whereby a coding sequence within said polynucleotide can be transcribed and translated in a host cell, and at least one of said control elements is heterologous to said coding sequence.

115. A recombinant vector comprising: (a) a polynucleotide according to claim 108; and (b) control elements that are operably linked to said polynucleotide whereby a coding sequence within said polynucleotide can be transcribed and translated in a host cell, and at least one of said control elements is heterologous to said coding sequence.

116. A recombinant vector comprising: (a) a polynucleotide according to claim 109; and (b) control elements that are operably linked to said polynucleotide whereby a coding sequence within said polynucleotide can be transcribed and translated in a host cell, and at least one of said control elements is heterologous to said coding sequence.

117. A recombinant vector comprising: (a) a polynucleotide according to claim 110; and (b) control elements that are operably linked to said polynucleotide whereby a coding sequence within said polynucleotide can be transcribed and translated in a host cell, and at least one of said control elements is heterologous to said coding sequence.

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	FIG	Draw D.
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☐ 3. Document ID: US 6797272 B1

L12: Entry 3 of 15

File: USPT

Sep 28, 2004

DOCUMENT-IDENTIFIER: US 6797272 B1

TITLE: Enhanced immunogenicity using leukotoxin chimeras

CLAIMS:

1. A chimeric protein comprising an antigen coupled to a carrier protein, wherein said carrier protein is a leukotoxin polypeptide that activates helper T-cells and said antigen is a selected peptide hormone which is not a cytokine, and further wherein said leukotoxin polypeptide is an RTX leukotoxin from a bacterium selected from the group consisting of Pasteurella haemolytica, E. coli and Actinobacillus pleuropneumoniae.
2. The chimeric protein of claim 1, wherein said leukotoxin polypeptide is coupled to gonadotropin releasing hormone (GnRH) or an epitope thereof.
3. The chimeric protein of claim 2, comprising the amino acid sequence of SEQ ID NO:12.
4. The chimeric protein of claim 1, wherein the leukotoxin polypeptide is a Pasteurella haemolytica leukotoxin polypeptide.
5. The chimeric protein of claim 2, wherein the leukotoxin polypeptide is a Pasteurella haemolytica leukotoxin polypeptide.

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	Index	Drawings
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☐ 4. Document ID: US 6369201 B1

L12: Entry 4 of 15

File: USPT

Apr 9, 2002

DOCUMENT-IDENTIFIER: US 6369201 B1

TITLE: Myostatin multimers

CLAIMS:

5. The myostatin multimer of claim 1, wherein said myostatin immunogens are myostatin peptides and said multimer comprises a molecule according to the general formula (MP-X-MP)_y, wherein MP is a myostatin peptide, X is selected from the group consisting of a peptide linkage, an amino acid spacer group, a leukotoxin polypeptide and [MP]_{sub.n}, where n is greater than or equal to 1, and y is greater than or equal to 1.
10. The myostatin multimer of claim 9, wherein said multimer comprises six copies of SEQ ID NO:4 fused to LKT 114 as depicted in FIGS. 15A-15D (SEQ ID NO:26).
12. The myostatin multimer of claim 1, wherein said multimer comprises eight copies of SEQ ID NO:6 fused to LKT 114 as depicted in FIGS. 15A-15D (SEQ ID NO:26).

14. The myostatin multimer of claim 13, wherein said multimer comprises eight copies of SEQ ID NO:8 fused to LKT 114 as depicted in FIGS. 15A-15D (SEQ ID NO:26).
16. The myostatin multimer of claim 15, wherein said multimer comprises eight copies of SEQ ID NO:10 fused to LKT 114 as depicted in FIGS. 15A-15D (SEQ ID NO:26).
18. The myostatin multimer of claim 17, wherein said multimer comprises six copies of SEQ ID NO:12 fused to LKT 114 as depicted in FIGS. 15A-15D (SEQ ID NO:26).
20. The myostatin multimer of claim 19, wherein said multimer comprises four copies of SEQ ID NO:14 fused to LKT 114 as depicted in FIGS. 15A-15D (SEQ ID NO:26).
22. The myostatin multimer of claim 21, wherein said multimer comprises six copies of SEQ ID NO:16 fused to LKT 114 as depicted in FIGS. 15A-15D (SEQ ID NO:26).
24. The myostatin multimer of claim 23, wherein said multimer comprises four copies of SEQ ID NO:18 fused to LKT 114 as depicted in FIGS. 15A-15D (SEQ ID NO:26).
26. The myostatin multimer of claim 25, wherein said multimer comprises eight copies of SEQ ID NO:20 fused to LKT 114 as depicted in FIGS. 15A-15D (SEQ ID NO:26).
28. The myostatin multimer of claim 27, wherein said multimer comprises four copies of SEQ ID NO:22 fused to LKT 114 as depicted in FIGS. 15A-15D (SEQ ID NO:26).

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	INDEX	Drawings
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☐ 5. Document ID: US 6180112 B1

L12: Entry 5 of 15

File: USPT

Jan 30, 2001

DOCUMENT-IDENTIFIER: US 6180112 B1
TITLE: Pasteurella haemolytica vaccine

CLAIMS:

1. A whole cell vaccine composition comprising a therapeutically effective amount of recombinant Pasteurella haemolytica organism comprising an inactivated lktC gene, wherein said recombinant Pasteurella haemolytica organism expresses inactive leukotoxin, wherein and said inactive leukotoxin comprises proleukotoxin.
4. The vaccine composition of claim 1, wherein said recombinant Pasteurella haemolytica comprises an lktC::cat operon fusion.
5. The vaccine composition of claim 1, wherein said expression of inactive leukotoxin is stably maintained.
6. The vaccine composition of claim 1, wherein said recombinant Pasteurella haemolytica contains an activator for expression of said inactive leukotoxin.
8. The vaccine composition of claim 1, wherein said recombinant Pasteurella haemolytica further comprises a strong leukotoxin promoter.

9. A whole cell composition comprising recombinant *Pasteurella haemolytica* organism comprising an inactivated lktC gene, wherein said recombinant *Pasteurella haemolytica* organism expresses inactive leukotoxin, and wherein said inactive leukotoxin comprises proleukotoxin.

12. The composition of claim 9, wherein said recombinant *Pasteurella haemolytica* comprises an lktC::cat operon fusion.

13. The composition of claim 9, wherein said expression of inactive leukotoxin is stably maintained.

14. The composition of claim 9, wherein said recombinant *Pasteurella haemolytica* contains an activator for expression of said inactive leukotoxin.

16. The composition of claim 9, wherein said recombinant *Pasteurella haemolytica* further comprises a strong leukotoxin promoter.

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	Index	Drawings
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☐ 6. Document ID: US 6096320 A

L12: Entry 6 of 15

File: USPT

Aug 1, 2000

DOCUMENT-IDENTIFIER: US 6096320 A

TITLE: Vaccines with chimeric protein comprising gamma-interferon and leukotoxin derived from *Pasteurella haemolytica*

CLAIMS:

1. A vaccine composition comprising an immunogenic chimeric protein that comprises gamma-interferon (.gamma.IFN), or an active fragment thereof, linked to at least one epitope of a leukotoxin derived from *Pasteurella haemolytica*, and a pharmaceutically acceptable vehicle.

2. The vaccine composition of claim 1 wherein said chimeric protein is linked to carrier.

4. The vaccine composition of claim 1, wherein said leukotoxin is full-length P. *haemolytica* leukotoxin.

5. The vaccine composition of claim 1, wherein said leukotoxin is a truncated leukotoxin that lacks cytotoxic activity.

6. The vaccine composition of claim 5, wherein said truncated leukotoxin is LKT 352.

8. The vaccine composition of claim 7, wherein said chimeric protein comprises an amino acid sequence (a) encoded by a polynucleotide that encodes the LKT-.gamma.IFN amino acid sequence of SEQ ID NO:4, or (b) encoded by a polynucleotide that hybridizes to the polynucleotide of (a) under stringent hybridization conditions.

12. The vaccine composition of claim 8, wherein said chimeric protein comprises the LKT-.gamma.IFN amino acid sequence of SEQ ID NO:4.

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	LMC	Drawings
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☐ 7. Document ID: US 5969126 A

L12: Entry 7 of 15

File: USPT

Oct 19, 1999

DOCUMENT-IDENTIFIER: US 5969126 A

TITLE: GNRH-leukotoxin chimeras

CLAIMS:

1. A DNA construct encoding a chimeric protein comprising a leukotoxin polypeptide fused to a multimer having more than one selected gonadotropin releasing hormone (GnRH) polypeptide, said DNA construct comprising a first nucleotide sequence encoding a leukotoxin polypeptide operably linked to a second nucleotide sequence encoding a GnRH multimer.
4. A DNA construct encoding a chimeric protein, wherein the chimeric protein comprises a leukotoxin polypeptide fused to first and second multimers wherein the C-terminus of the first multimer is fused to the N-terminus of the leukotoxin polypeptide and the N-terminus of the second multimer is fused to the C-terminus of the leukotoxin polypeptide, and further wherein each of said multimers comprises more than one selected gonadotropin releasing hormone (GnRH) polypeptide, said DNA construct comprising:

a first nucleotide sequence encoding the first GnRH multimer; and

a second nucleotide sequence encoding the second GnRH multimer;

wherein said first and second nucleotide sequences are operably linked by a third nucleotide sequence encoding a leukotoxin polypeptide.
12. A DNA construct encoding a chimeric protein comprising a leukotoxin polypeptide fused to a multimer having eight selected gonadotropin releasing hormone (GnRH) polypeptides, wherein the C-terminus of the leukotoxin polypeptide is fused to the N-terminus of the multimer.
13. The DNA construct of claim 12, wherein the leukotoxin polypeptide comprises the 52 kD LKT 111 carrier polypeptide, as depicted at amino acid positions 11-491, inclusive, of SEQ ID NO:10.
14. A DNA construct encoding a chimeric protein comprising a leukotoxin polypeptide fused to a multimer having eight selected gonadotropin releasing hormone (GnRH) polypeptides, wherein the C-terminus of the multimer is fused to the N-terminus of the leukotoxin polypeptide.
15. The DNA construct of claim 14, wherein the leukotoxin polypeptide comprises the 52 kD LKT 111 carrier polypeptide, as depicted at amino acid positions 11-491, inclusive, of SEQ ID NO:10.

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	Full	Grant
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☐ 8. Document ID: US 5874279 A

L12: Entry 8 of 15

File: USPT

Feb 23, 1999

DOCUMENT-IDENTIFIER: US 5874279 A

TITLE: Recombinant infectious bovine rhinotracheitis virus

CLAIMS:

7. The live recombinant infectious bovine rhinotracheitis virus of claim 1, wherein the foreign DNA encodes a polypeptide which is selected from a group consisting of Bovine Respiratory Syncytial Virus fusion protein, Bovine Respiratory Syncytial Virus attachment protein, Bovine Respiratory Syncytial Virus nucleocapsid protein, Parainfluenza type 3 fusion protein, Bovine Viral Diarrhea Virus glycoprotein 53, and P Haemolytica Leukotoxin.

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	Full	Grant
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☐ 9. Document ID: US 5849531 A

L12: Entry 9 of 15

File: USPT

Dec 15, 1998

DOCUMENT-IDENTIFIER: US 5849531 A

TITLE: Compositions and treatments for pneumonia in animals

CLAIMS:

1. An isolated nucleic acid molecule comprising a nucleotide sequence that encodes an immunogenic Pasteurella haemolytica leukotoxin polypeptide, wherein said leukotoxin polypeptide has a truncation selected from the group consisting of an N-terminal truncation, a C-terminal truncation, and an N-terminal and C-terminal truncation of the native full length sequence and further wherein said leukotoxin polypeptide comprises the amino acid sequence encoded by the leukotoxin gene present in plasmid pAA342 (ATCC Accession no. 98265), or a nucleic acid molecule that hybridizes thereto under stringent conditions.

2. The nucleic acid molecule of claim 1 wherein said truncated leukotoxin is LKT 352 having an amino acid sequence as depicted at positions 11-923, inclusive, of FIGS. 5A-5F, or a nucleic acid molecule that hybridizes thereto under stringent conditions.

3. A DNA construct comprising an expression cassette comprised of:

(a) the nucleic acid molecule of claim 2; and

(b) control sequences that are operably linked to said nucleic acid molecule whereby said nucleic acid molecule can be transcribed and translated in a host cell, and further wherein at least one of said control sequences is heterologous to

said nucleic acid molecule.

6. A DNA construct comprising an expression cassette comprised of:

(a) the nucleic acid molecule of claim 1; and

(b) control sequences that are operably linked to said nucleic acid molecule whereby said nucleic acid molecule can be transcribed and translated in a host cell, and further wherein at least one of said control sequences is heterologous to said nucleic acid molecule.

9. The nucleic acid molecule of claim 1 wherein said truncated leukotoxin is encoded by the leukotoxin gene present in plasmid pAA342.

10. A DNA construct comprising an expression cassette comprised of:

(a) the nucleic acid molecule of claim 9; and

(b) control sequences that are operably linked to said nucleic acid molecule whereby said nucleic acid molecule can be transcribed and translated in a host cell, and further wherein at least one of said control sequences is heterologous to said nucleic acid molecule.

13. The nucleic acid molecule of claim 1 wherein said truncated leukotoxin is encoded by the leukotoxin gene present in plasmid pAA101 and has an amino acid sequence as depicted at positions 1-377, inclusive, of FIG. 3.

14. A DNA construct comprising an expression cassette comprised of:

(a) the nucleic acid molecule of claim 13; and

(b) control sequences that are operably linked to said nucleic acid molecule whereby said nucleic acid molecule can be transcribed and translated in a host cell, and further wherein at least one of said control sequences is heterologous to said nucleic acid molecule.

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	Drawings	Table
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☐ 10. Document ID: US 5837268 A

L12: Entry 10 of 15

File: USPT

Nov 17, 1998

DOCUMENT-IDENTIFIER: US 5837268 A

TITLE: GnRH-leukotoxin chimeras

CLAIMS:

1. A chimeric protein comprising a leukotoxin polypeptide fused to first and second multimers, wherein the C-terminus of the first multimer is fused to the N-terminus of the leukotoxin polypeptide and the N-terminus of the second multimer is fused to the C-terminus of the leukotoxin polypeptide, and further wherein each of said multimers comprises more than one selected GnRH polypeptide.

2. The chimeric protein of claim 1 wherein the first and second GnRH multimers are different and comprise molecules according to the general formula [GnRH-X-GnRH].sub.n, wherein:

GnRH comprises a GnRH polypeptide;

X is selected from the group consisting of a peptide linkage, an amino acid spacer group and a leukotoxin polypeptide; and

n is an integer greater than or equal to 1.

3. The chimeric protein of claim 1 wherein the first and second GnRH multimers are the same and comprise molecules according to the general formula [GnRH-X-GnRH].sub.n, wherein:

GnRH comprises a GnRH polypeptide;

X is selected from the group consisting of a peptide linkage, an amino acid spacer group and a leukotoxin polypeptide; and

n is an integer greater than or equal to 1.

4. The chimeric protein of claim 3 wherein X is an amino acid spacer group having at least one helper T-cell epitope.

5. The chimeric protein of claim 3 wherein n is 4.

6. The chimeric protein of claim 1 wherein the leukotoxin polypeptide lacks cytotoxic activity.

7. The chimeric protein of claim 6 wherein the leukotoxin polypeptide is the polypeptide depicted at amino acid residues 11-923 of SEQ ID NO:6.

8. The chimeric protein of claim 6 wherein the leukotoxin polypeptide is the polypeptide depicted at amino acid residues 11-491 of SEQ ID NO:10.

9. The chimeric protein of claim 6 wherein the leukotoxin polypeptide is SEQ ID NO:17.

10. The chimeric protein of claim 3 wherein the first multimer further comprises the amino acid sequence (Met-Ala-Thr-Val-Ile-Asp-Arg-Ser SEQ ID NO:21) fused to the N-terminus thereof.

11. The chimeric protein of claim 1 comprising the amino acid sequence depicted in FIGS. 9-1 through 9-6 (SEQ ID NO:15 and SEQ ID NO:16).

12. A vaccine composition comprising the chimeric protein of claim 1 and a pharmaceutically acceptable vehicle.

13. A vaccine composition comprising the chimeric protein of claim 3 and a pharmaceutically acceptable vehicle.

14. A vaccine composition comprising the chimeric protein of claim 5 and a pharmaceutically acceptable vehicle.

15. A vaccine composition comprising the chimeric protein of claim 6 and a pharmaceutically acceptable vehicle.

16. A vaccine composition comprising the chimeric protein of claim 11 and a pharmaceutically acceptable vehicle.

Full	Title	Citation	Front	Review	Classification	Date	Reference	Abstract	Claims	Footnote	Drawings
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☐ 11. Document ID: US 5723129 A

L12: Entry 11 of 15

File: USPT

Mar 3, 1998

DOCUMENT-IDENTIFIER: US 5723129 A

TITLE: GnRH-leukotoxin chimeras

CLAIMS:

1. A chimeric protein comprising a leukotoxin polypeptide fused to a multimer having more than one selected GnRH polypeptide, whereby said leukotoxin portion of said chimeric protein acts to increase the immunogenicity of said GnRH multimer.
2. The chimeric protein of claim 1 wherein said leukotoxin polypeptide lacks leukotoxic activity.
3. The chimeric protein of claim 2 wherein said leukotoxin is LKT 352.
4. The chimeric protein of claim 2 wherein said leukotoxin is LKT 111.
5. The chimeric protein of claim 1 wherein said GnRH multimer comprises a molecule according to the general formula GnRH-X-GnRH wherein X is selected from the group consisting of a peptide linkage, an amino acid spacer group, a leukotoxin polypeptide and [GnRH].sub.n where n is greater than or equal to 1, and further wherein GnRH comprises any GnRH polypeptide.
6. The chimeric protein of claim 5 wherein X comprises an amino acid spacer group including at least one helper T-cell epitope.
7. The chimeric protein of claim 1 wherein said chimeric protein comprises the amino acid sequence depicted in FIGS. 5A-5h, SEQ ID NOS:7-8.
8. The chimeric protein of claim 1 wherein said chimeric protein comprises the amino acid sequence depicted in FIGS. 7A-7E, SEQ ID NOS:9-10.
9. A vaccine composition comprising the chimeric protein of claim 1 and a pharmaceutically acceptable vehicle.
10. A vaccine composition comprising the chimeric protein of claim 2 and a pharmaceutically acceptable vehicle.
11. A vaccine composition comprising the chimeric protein of claim 5 and a pharmaceutically acceptable vehicle.
12. A vaccine composition comprising the chimeric protein of claim 7 and a pharmaceutically acceptable vehicle.
13. A vaccine composition comprising the chimeric protein of claim 8 and a pharmaceutically acceptable vehicle.

19. A chimeric protein comprising a leukotoxin polypeptide fused to a multimer having eight selected GnRH polypeptides, wherein the C-terminus of the leukotoxin polypeptide is fused to the N-terminus of the multimer.
20. The chimeric protein of claim 19, wherein the leukotoxin polypeptide comprises the 52 kD LKT 111 carrier polypeptide.
21. A chimeric protein comprising a leukotoxin polypeptide fused to a multimer having eight selected GnRH polypeptides, wherein the C-terminus of the multimer is fused to the N-terminus of the leukotoxin polypeptide.
22. The chimeric protein of claim 21, wherein the leukotoxin polypeptide comprises the 52 kD LKT 111 carrier polypeptide.
23. A vaccine composition comprising the chimeric protein of claim 19 and a pharmaceutically acceptable vehicle.
24. A vaccine composition comprising the chimeric protein of claim 20 and a pharmaceutically acceptable vehicle.
25. A vaccine composition comprising the chimeric protein of claim 21 and a pharmaceutically acceptable vehicle.
26. A vaccine composition comprising the chimeric protein of claim 22 and a pharmaceutically acceptable vehicle.

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	EMC	Grant
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☐ 12. Document ID: US 5708155 A

L12: Entry 12 of 15

File: USPT

Jan 13, 1998

DOCUMENT-IDENTIFIER: US 5708155 A

TITLE: Enhanced immunogenicity using leukotoxin chimeras

CLAIMS:

1. A DNA construct encoding a chimeric protein, said DNA construct comprising a first nucleotide sequence encoding a leukotoxin polypeptide capable of activating helper T-cells directed to a selected antigen, operably linked to a second nucleotide sequence encoding said selected antigen.

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	EMC	Grant
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☐ 13. Document ID: US 5594107 A

L12: Entry 13 of 15

File: USPT

Jan 14, 1997

DOCUMENT-IDENTIFIER: US 5594107 A

**** See image for Certificate of Correction ****

TITLE: Chimeric protein comprising an RTX-family cytotoxin and interferon-2 or interferon

CLAIMS:

1. An immunogenic chimeric protein comprising a cytokine selected from the group consisting of interleukin-2 (IL2), and gamma-interferon (.gamma.IFN), linked to at least one epitope of an RTX cytotoxin which comprises the amino acid sequence Gly-Gly-X-Gly-(Asn or Asp)-Asp (SEQ ID NO: 5), wherein X is selected from the group consisting of an aliphatic amino acid, and a charged amino acid or its corresponding neutral amino acid.
2. The chimeric protein of claim 1 wherein X is selected from the group consisting of Lys, Asp, Val, and Asn.
3. The chimeric protein of claim 1 wherein said RTX cytotoxin is a leukotoxin.
4. The chimeric protein of claim 3 wherein said leukotoxin is derived from P. haemolytica.
5. The chimeric protein of claim 4 wherein said leukotoxin is full-length P. haemolytica leukotoxin.
6. The chimeric protein of claim 3 wherein said leukotoxin is a truncated leukotoxin which lacks leukotoxic activity.
7. The chimeric protein of claim 6 wherein said truncated leukotoxin is LKT 352.
8. The chimeric protein of claim 1 wherein said cytokine is interleukin-2 (IL2), or an active fragment thereof.
9. The chimeric protein of claim 8 wherein said IL2 is bovine IL2, or an active fragment thereof.
10. The chimeric protein of claim 9 comprising the amino acid sequence depicted in FIG. 3 (SEQ ID NOS: 1-2).
11. The chimeric protein of claim 1 wherein said cytokine is gamma-interferon (.gamma.IFN), or an active fragment thereof.
12. The chimeric protein of claim 11 wherein said .gamma.IFN is bovine .gamma.IFN, or an active fragment thereof.
13. The chimeric protein of claim 12 comprising the amino acid sequence depicted in FIG. 7 (SEQ ID NOS: 3-4).

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	FIGS	Drawings
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☐ 14. Document ID: US 5422110 A

L12: Entry 14 of 15

File: USPT

Jun 6, 1995

DOCUMENT-IDENTIFIER: US 5422110 A

TITLE: Enhanced immunogenicity using leukotoxin chimeras

CLAIMS:

1. An immunological carrier system comprising a chimeric protein, said chimeric protein consisting of a leukotoxin molecule which lacks leukotoxic activity, fused to somatostatin (SRIF), whereby said leukotoxin of said chimeric protein acts to increase the immunogenicity of said SRIF.
5. An immunological carrier system comprising a chimeric protein, said chimeric protein consisting of a leukotoxin molecule which lacks leukotoxic activity, fused to gonadotropin releasing hormone (GnRH), whereby said leukotoxin of said chimeric protein acts to increase the immunogenicity of said GnRH.
6. The carrier system of claim 5 wherein said chimeric protein consists of the amino acid sequence depicted in FIG. 8 (SEQ ID NO:9).
7. A vaccine composition comprising the chimeric protein of claim 5 and a pharmaceutically acceptable vehicle.
9. An immunological carrier system comprising a chimeric protein, said chimeric protein consisting of a leukotoxin molecule which lacks leukotoxic activity, fused to bovine rotavirus VP4, whereby said leukotoxin of said chimeric protein acts to increase the immunogenicity of said VP4.

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	FIGS	Drawings
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☐ 15. Document ID: US 5273889 A

L12: Entry 15 of 15

File: USPT

Dec 28, 1993

DOCUMENT-IDENTIFIER: US 5273889 A

**** See image for Certificate of Correction ****

TITLE: Gamma-interferon-leukotoxin gene fusions and uses thereof

CLAIMS:

1. A DNA construct comprising a first nucleotide sequence encoding gamma-interferon (.gamma.IFN), operably linked to a second nucleotide sequence encoding an immunogenic leukotoxin, wherein said leukotoxin is characterized by having the amino acid sequence G-G-X-G-X-D (SEQ ID NO. 3) where X is K, D, V or N.
4. The DNA construct of claim 1 wherein said leukotoxin is a P. haemolytica leukotoxin.
5. The DNA construct of claim 1 wherein said leukotoxin is a truncated leukotoxin as present in plasmid pAA352 (ATCC Accession No. 68283).
7. A vector comprising a DNA construct encoding a gamma-interferon-leukotoxin fusion protein, wherein the plasmid is pAA497.

□ 1: Microbiology. 1996 Sep;142 (Pt 9):2499-507.

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Characterization of epitopes involved in the neutralization of *Pasteurella haemolytica* serotype A1 leukotoxin.

Lainson FA, Murray J, Davies RC, Donachie W.

Moredun Research Institute, Edinburgh, UK.

Defined segments of the leukotoxin A gene (lktA) from an A1 serotype of *Pasteurella haemolytica* were cloned into a plasmid vector and expressed as LacZ alpha fusion proteins. These fusion proteins were electrophoresed in SDS-PAGE gels and their immunoblotting reactivities with several monoclonal antibodies characterized. The epitope recognized by a strongly neutralizing monoclonal antibody was localized to a 32 amino acid region near the C terminus of the leukotoxin A (LktA) molecule. The epitope recognized by a non-neutralizing antibody was localized to a 33 amino acid region immediately adjacent. Smaller recombinant peptides containing these epitopes were not antigenic, but a polypeptide encompassing 229 amino acids at the C terminus evoked neutralizing antibodies when used to immunize specific-pathogen-free lambs. The distributions of linear epitopes recognized by this antiserum and by antisera raised to full-length recombinant LktA and to native LktA produced by *P. haemolytica* serotype A1 were determined by their reactivities with a set of overlapping 10 amino acid synthetic peptides. This revealed a complex distribution of linear epitopes at the C-terminal end of LktA. Toxin-neutralizing antibodies in convalescent sheep serum were shown to be directed against conformational epitopes by selective absorption of antibodies directed against linear epitopes.

PMID: 8828217 [PubMed - indexed for MEDLINE]

DOCUMENT-IDENTIFIER: US 5969126 A
TITLE: GNRH-leukotoxin chimeras

CLAIMS:

1. A DNA construct encoding a chimeric protein comprising a leukotoxin polypeptide fused to a multimer having more than one selected gonadotropin releasing hormone (GnRH) polypeptide, said DNA construct comprising a first nucleotide sequence encoding a leukotoxin polypeptide operably linked to a second nucleotide sequence encoding a GnRH multimer.

4. A DNA construct encoding a chimeric protein, wherein the chimeric protein comprises a leukotoxin polypeptide fused to first and second multimers wherein the C-terminus of the first multimer is fused to the N-terminus of the leukotoxin polypeptide and the N-terminus of the second multimer is fused to the C-terminus of the leukotoxin polypeptide, and further wherein each of said multimers comprises more than one selected gonadotropin releasing hormone (GnRH) polypeptide, said DNA construct comprising:

a first nucleotide sequence encoding the first GnRH multimer; and

a second nucleotide sequence encoding the second GnRH multimer;

wherein said first and second nucleotide sequences are operably linked by a third nucleotide sequence encoding a leukotoxin polypeptide.

12. A DNA construct encoding a chimeric protein comprising a leukotoxin polypeptide fused to a multimer having eight selected gonadotropin releasing hormone (GnRH) polypeptides, wherein the C-terminus of the leukotoxin polypeptide is fused to the N-terminus of the multimer.

13. The DNA construct of claim 12, wherein the leukotoxin polypeptide comprises the 52 kD LKT 111 carrier polypeptide, as depicted at amino acid positions 11-491, inclusive, of SEQ ID NO:10.

14. A DNA construct encoding a chimeric protein comprising a leukotoxin polypeptide fused to a multimer having eight selected gonadotropin releasing hormone (GnRH) polypeptides, wherein the C-terminus of the multimer is fused to the N-terminus of the leukotoxin polypeptide.

15. The DNA construct of claim 14, wherein the leukotoxin polypeptide comprises the 52 kD LKT 111 carrier polypeptide, as depicted at amino acid positions 11-491, inclusive, of SEQ ID NO:10.

fragment

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If your question is not covered, please contact <helpdesk@expasy.org>.

NCBI BLAST program reference [PMID:9254694]:
Altschul S.F., Madden T.L., Schäffer A.A., Zhang J., Zhang Z., Miller W., Lipman D.J. Gapped BLAST and PSI-BLAST: a new generation of protein database search programs. Nucleic Acids Res. 25:3389-3402(1997).

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Query: 927 AA (of which 8% low-complexity regions filtered out)
Date run: 2006-03-27 16:58:36 UTC+0100 on blast01.vital-it.ch
Program: NCBI BLASTP 2.2.13 [Nov-27-2005]
Database: UniProtKB

2,893,171 sequences; 943,878,704 total letters
UniProt Knowledgebase Release 7.3 consists of:
UniProtKB/Swiss-Prot Release 49.3 of 21-Mar-2006: 212425 entries
UniProtKB/TrEMBL Release 32.3 of 21-Mar-2006: 2666963 entries

List of potentially matching sequences

Send selected sequences to

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Db	AC	Description
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<input type="checkbox"/>	tr Q93GI2	_MORBO RTX toxin [mbxA] [Moraxella bovis]
--------------------------	-----------	---

<input type="checkbox"/>	sp Q9ETX2	LKTA_MANGL Leukotoxin (Lkt) [lktA] [Mannheimia glucosida]
--------------------------	-----------	---

☐ tr Q6TB03 _9PAST Leukotoxin structural protein [lktA] [Mannheimia]
☐ sp P55118 LKA11_PASHA Leukotoxin (Lkt) [lktA] [Pasteurella haemo.
☐ sp Q7BHI8 LKA1B_PASHA Leukotoxin (Lkt) [lktA] [Pasteurella haemo.
☐ sp P16535 LKA1A_PASHA Leukotoxin (Lkt) [lktA] [Pasteurella haemo.
☐ sp P0C083 LKTA6_PASHA Leukotoxin (Lkt) [lktA] [Pasteurella haemo.
☐ sp P0C084 LKA7A_PASHA Leukotoxin (Lkt) [lktA] [Pasteurella haemo.
☐ sp Q9EV29 LKA2D_PASHA Leukotoxin (Lkt) [lktA] [Pasteurella haemo.
☐ sp Q9EV32 LKA16_PASHA Leukotoxin (Lkt) [lktA] [Pasteurella haemo.
☐ sp Q9EV34 LKTA8_PASHA Leukotoxin (Lkt) [lktA] [Pasteurella haemo.
☐ sp Q9EV33 LKA14_PASHA Leukotoxin (Lkt) [lktA] [Pasteurella haemo.
☐ sp Q9EV31 LKA13_PASHA Leukotoxin (Lkt) [lktA] [Pasteurella haemo.
☐ sp P0C085 LKA7B_PASHA Leukotoxin (Lkt) [lktA] [Pasteurella haemo.
☐ sp Q9EV27 LKA2E_PASHA Leukotoxin (Lkt) [lktA] [Pasteurella haemo.
☐ sp Q9EV30 LKA2A_PASHA Leukotoxin (Lkt) [lktA] [Pasteurella haemo.
☐ sp P0C082 LKA2C_PASHA Leukotoxin (Lkt) [lktA] [Pasteurella haemo.
☐ sp P0C081 LKA2B_PASHA Leukotoxin (Lkt) [lktA] [Pasteurella haemo.
☐ sp P55123 LKTA_PASSP Leukotoxin (PlLkt) [lktA] [Pasteurella haem.
☐ sp P55117 LKTA_PASTR Leukotoxin (Lkt) [lktA] [Pasteurella trehal.
☐ tr Q5DI89 _9PAST ApxIIA [apxIIA] [Actinobacillus porcitisillarum]
☐ tr Q84C02 _ACTPL ApxIIA [Actinobacillus pleuropneumoniae (Haemoph
☐ sp P15377 RTX2A_ACTPL RTX-II toxin determinant A (APX-IIA) (Hemo.
☐ tr Q93NP1 _ACTPL RTX toxin IIA [Actinobacillus pleuropneumoniae (
☐ tr Q5XUT6 _ACTPL ApxIIA [apxIIA] [Actinobacillus pleuropneumoniae
☐ sp Q00951 HLYA_ACTSU Hemolysin (Cytolysin II) (CLY-IIA) (HLY-IIA.
☐ tr Q8KWZ6 _ACTEU AqxA [aqxA] [Actinobacillus equuli]
☐ tr Q8KWZ9 _9PAST AqxA [aqxA] [Actinobacillus cf. equuli]
☐ sp Q9RCG8 PAXA_PASAE Exotoxin paxA [paxA] [Pasteurella aerogenes]
☐ tr Q93NP0 _ACTPL RTX-toxin IIIA [Actinobacillus pleuropneumoniae
☐ sp P55131 RTX32_ACTPL RTX-III toxin determinant A from serotype .
☐ sp P55130 RTX31_ACTPL RTX-III toxin determinant A from serotype .
☐ tr Q6TB11 _9PAST Leukotoxin structural protein (Fragment) [lktA]
☐ tr Q6TB07 _9PAST Leukotoxin structural protein (Fragment) [lktA]
☐ tr Q8FE01 _ECOL6 Hemolysin A [hlyA] [Escherichia coli O6]
☐ tr Q8GA40 _ECOLI Hemolysin A [hlyA] [Escherichia coli]
☐ tr Q8G9Z4 _ECOLI HlyA protein [hlyA] [Escherichia coli]
☐ sp P09983 HLYAC_ECOLI Hemolysin, chromosomal [hlyA] [Escherichia.
☐ sp P08715 HLYAP_ECOLI Hemolysin, plasmid [hlyA] [Escherichia coli
☐ tr Q548V0 _ACTPL ApxIA [apxIA] [Actinobacillus pleuropneumoniae (
☐ tr Q93NP2 _ACTPL RTX toxin IA [Actinobacillus pleuropneumoniae (H
☐ tr Q3ZU04 _ECOLI Hemolysin A [ehxA] [Escherichia coli]
☐ tr O85101 _ECOLI Hemolysin [ehxA] [Escherichia coli]
☐ tr Q9LC58 _ECOLI Hemolysin A [EHEC-hlyA] [Escherichia coli]

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Note: most headings are clickable, even if they don't appear as links. They link to the user manual or other documents.

Entry information

Entry name **LKA11_PASHA**
 Primary accession number **P55118**
 Secondary accession numbers **None**
 Integrated into Swiss-Prot on **October 1, 1996**
 Sequence was last modified on **October 1, 1996 (Sequence version 1)**
 Annotations were last modified on **March 21, 2006 (Entry version 39)**

Name and origin of the protein

Protein name **Leukotoxin**
 Synonym **Lkt**
 Gene name **Name: lktA**
 From **Pasteurella haemolytica (Mannheimia haemolytica)** [TaxID: 75985]
 Taxonomy **Bacteria; Proteobacteria; Gammaproteobacteria; Pasteurellales; Pasteurellaceae; Mannheimia.**

References

[1] NUCLEOTIDE SEQUENCE [GENOMIC DNA].

STRAIN=Serotype A11;

PubMed=8225575 [NCBI, ExPASy, EBI, Israel, Japan]

Burrows L.L., Olah-Winfield E., Lo R.Y.C.;

"Molecular analysis of the leukotoxin determinants from Pasteurella haemolytica serotype 16.";

Infect. Immun. 61:5001-5007(1993).

Comments

- **FUNCTION:** Pasteurella leukotoxins are exotoxins that attack host leukocytes and especially polymorphonuclear cells, by causing cell rupture. The leukotoxin binds to the host LFA-integrin and induces a signaling cascade leading to many biological effects, including tyrosine phosphorylation of the CD18 tail, elevation of the intracellular Ca(2+) and lysis

host cell (*By similarity*). This leukotoxin is a major contributor to the pathogenesis of lung injury in ovine pneumonic pasteurellosis. It has also weak hemolytic activity.

- **SUBCELLULAR LOCATION:** Secreted protein (*By similarity*).
- **DOMAIN:** The transmembrane domains are believed to be involved in pore formation in target cells (*By similarity*).
- **DOMAIN:** The Gly-rich region is probably involved in calcium binding, which is required for target cell-binding and cytolytic activity (*By similarity*).
- **DOMAIN:** The C-terminal domain contains an export signal that is recognized by the ABC transporter complex IktBD (*By similarity*).
- **PTM:** Acylated by IktC. The toxin only becomes active when modified (*By similarity*).
- **MISCELLANEOUS:** The IktCABD operon has a complex mosaic structure that has been derived by extensive inter- and intraspecies horizontal DNA transfer and intragenic recombination events.
- **SIMILARITY:** Belongs to the RTX prokaryotic toxin (TC 1.C.11) family [view classification]
- **SIMILARITY:** Contains 5 hemolysin-type calcium-binding repeats.

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Cross-references

Sequence databases

EMBL	U01215; AAB36689.1; -;	[EMBL / GenBank / DDBJ]
	Unassigned_DNA.	[CodingSequence]

3D structure databases

ModBase P55118.

Protein-protein interaction databases

DIP P55118.

2D gel databases

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Organism-specific gene databases

HOGENOM [Family / Alignment / Tree]

Family and domain databases

InterPro	IPR001343; Hemolysin_Ca_bd. IPR003995; RtxA. IPR011049; Serralysin_like_C. Graphical view of domain structure.
Pfam	PF00353; HemolysinCabind; 5. PF02382; RTX; 1. Pfam graphical view of domain structure.
PRINTS	PR00313; CABNDNGRPT. PR01488; RTXTOXINA.
PROSITE	PS00330; HEMOLYSIN_CALCIUM; 4.
ProDom	[Domain structure / List of seq. sharing at least 1 domain]
BLOCKS	P55118.

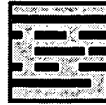
Other

ProtoNet P55118.

UniRef View cluster of proteins with at least 50% / 90% / 100% identity.

Keywords**Calcium; Cytolysis; Hemolysis; Lipoprotein; Membrane; Repeat; Toxin; Transmembran
Virulence.****Features**

Feature table viewer



Feature aligner

Key	From	To	Length	Description	FTId
CHAIN	1	953	953	Leukotoxin.	PRO_0000196230
TRANSMEM	230	250	21	Potential.	
TRANSMEM	297	317	21	Potential.	
TRANSMEM	381	401	21	Potential.	
REPEAT	715	732	18	Hemolysin-type calcium-binding 1.	
REPEAT	733	750	18	Hemolysin-type calcium-binding 2.	
REPEAT	751	768	18	Hemolysin-type calcium-binding 3.	
REPEAT	769	786	18	Hemolysin-type calcium-binding 4.	
REPEAT	789	806	18	Hemolysin-type calcium-binding 5.	

Sequence informationLength: **953 AA** [This is the length of the unprocessed precursor]Molecular weight: **102206 Da** [This is the MW of the unprocessed precursor]CRC64: **927FF56CFC884F12** is a checksum on the sequence

<u>10</u>	<u>20</u>	<u>30</u>	<u>40</u>	<u>50</u>	<u>60</u>
MGNKLTNIST	NLKSSWLTA	SGLNRTGQSL	AKAGQSLKTG	AKKIILYIPK	DYQYDTEKGN
<u>70</u>	<u>80</u>	<u>90</u>	<u>100</u>	<u>110</u>	<u>120</u>
GLQDLVKAAE	ELGIEVQKEE	GNDIAKAQTS	LGTIQNVLGL	TERGIVLSAP	QLDKLLQKTK
<u>130</u>	<u>140</u>	<u>150</u>	<u>160</u>	<u>170</u>	<u>180</u>
VGQAIGSAEN	LTKGFSSNAKT	VLSGIQSILG	SVLAGMDLDE	ALQKNSNELT	LAKAGLELTN
<u>190</u>	<u>200</u>	<u>210</u>	<u>220</u>	<u>230</u>	<u>240</u>
SLIENIANSV	KTLDAGDQI	NQLGSKLQNV	KGLSSLGDKL	KGLSGFDKTS	LGLDVVSGLL
<u>250</u>	<u>260</u>	<u>270</u>	<u>280</u>	<u>290</u>	<u>300</u>
SGATAALVLA	DKNASTSRKV	GAGFELANQV	VGNITKAVSS	YILAQRVAAG	LSSTGPVAAL
<u>310</u>	<u>320</u>	<u>330</u>	<u>340</u>	<u>350</u>	<u>360</u>
IASTVSLAIS	PLAFAGIADK	FNHAKSLESY	AERFKKLGYD	GDNLLAEYQR	GTGTIDRSVT
<u>370</u>	<u>380</u>	<u>390</u>	<u>400</u>	<u>410</u>	<u>420</u>
AINATALAAIA	GGVSAAGRGS	VIASPIALLV	SGITGVISTI	LQYSKQAMFE	HVANKIHNKI
<u>430</u>	<u>440</u>	<u>450</u>	<u>460</u>	<u>470</u>	<u>480</u>
VEWEKNNH GK	NYFENGYDAR	YLANLQDNMK	FLLNLNKLQ	AERVIAITQQ	QWDNNIGDLA


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      490      500      510      520      530      540
GISRLGEKVL SGKAYVDAFE EGKHLKADKL VQLDSANGII DVSNSGKAKT QDILFRTPLL

      550      560      570      580      590      600
TPGTDDRERV QTGKYEYITK LNINRVDSWK ITDGAASSTF DLTNVVQRIQ IELDNAGNVT

      610      620      630      640      650      660
KTKETKIVAK LGAGDDNVFV GSGTTEIDGG EGYDRVHYSR GNYGALTIDA TKETEQQGSYT

      670      680      690      700      710      720
VNRFBVETGKA LHEGTSTHTA LVGNREEKIE YRHSNNQHHA GYYTKDTLKA VEEIIGTSHN

      730      740      750      760      770      780
DIFKGSKFND AFNGGDGVDI IDGKDGNDRL FGGKGDDIID GGNGDDFIDG GKGNDLLHGG

      790      800      810      820      830      840
KGDDIFVHRQ GDGNDIITDS DGNDKLSFSD SNLKDLTFEK VKHNLVITNS RKEKVTIQDW

      850      860      870      880      890      900
FREADFAKEV RNYKATKDEK IEEIIGQNGE RITSKQVDDL IAKGNGKITQ DELSKVVDNY

      910      920      930      940      950
ELLKHSKNVT NSLDKLISSA SAFTSSNDSR NVLVAPTSML DQSLSSLQFA RAA

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DATE: Monday, March 27, 2006

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		<i>DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR</i>	
<input type="checkbox"/>	L1	(pasteurell\$ or leukotoxin or lkt or hemolytica or haemolytica).clm. and (fusion or recombinant or his6 or 6his to histag or his-tag or 6x or hishishishishishis).clm.	94
<input type="checkbox"/>	L2	rtx.clm. same fusion.clm.	1
<input type="checkbox"/>	L3	l1 and amalose	0
<input type="checkbox"/>	L4	l1 and xa	4
<input type="checkbox"/>	L5	fusion and xa and (leukotoxin or rtx or lkt or moraxella or pasteurella)	598
<input type="checkbox"/>	L6	fusion same(leukotoxin or rtx or lkt or moraxella or pasteurella)	174
<input type="checkbox"/>	L7	L6 and xa	28
<input type="checkbox"/>	L8	l1 and (hexahistidine or nickel or chelate or ninta or ni-nta or metal or 6his or hishishis)	42
<input type="checkbox"/>	L9	l6 and (hexahistidine or nickel or chelate or ninta or ni-nta or metal or 6his or hishishis)	78
<input type="checkbox"/>	L10	l6 same (hexahistidine or nickel or chelate or ninta or ni-nta or metal or 6his or hishishis)	1
<input type="checkbox"/>	L11	leukotoxi\$.clm.	49
<input type="checkbox"/>	L12	L11 and (fused or fusion or chimeric or heterologous or singlechain or single-chain).clm.	15

END OF SEARCH HISTORY

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	Index	Drawings
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Term	Documents
FUSED	199249
FUSEDs	0
FUSION	145005
FUSIONS	23822
CHIMERIC	49235
CHIMERICS	370
HETEROLOGOUS	49516
HETEROLOGOU	5
SINGLECHAIN	20
SINGLECHAINS	2
SINGLE-CHAIN	13354
(L11 AND (FUSED OR FUSION OR CHIMERIC OR HETEROLOGOUS OR SINGLECHAIN OR SINGLE-CHAIN) .CLM.) .PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD.	15

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□ 1: Mol Microbiol. 1993 Jan;7(2):285-8.

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Q pili enhance the attachment of *Moraxella bovis* to bovine corneas in vitro.

Ruehl WW, Marrs C, Beard MK, Shokooki V, Hinojoza JR, Banks S, Bieber D, Mattick JS.

Department of Pathology, Stanford University School of Medicine, California.

Moraxella bovis, the causative agent of infectious bovine keratoconjunctivitis, exhibits several virulence factors, including pili, haemolysin, leukotoxin, and proteases. The pili are filamentous appendages which mediate bacterial adherence. Prior studies have shown that Q-piliated *M. bovis* Epp63 are more infectious and more pathogenic than I-piliated and non-piliated isogenic variants, suggesting that Q pili per se, or traits associated with Q-pilin expression, promote the early association of Q-piliated bacteria with bovine corneal tissue. In order to better evaluate the role of Q pili in *M. bovis* attachment, several *M. bovis* strains and a recombinant *P. aeruginosa* strain which elaborates *M. bovis* Q pili but not *P. aeruginosa* PAK pili, were evaluated using an in vitro corneal attachment assay. For each strain tested, pilated organisms attached better than non-piliated bacteria. *M. bovis* Epp63 Q-piliated bacteria adhered better than either the I-piliated or non-piliated isogenic variants. Finally, recombinant *P. aeruginosa* organisms elaborating *M. bovis* Q pili adhered better than the parent *P. aeruginosa* strain which did not produce *M. bovis* pili. These results indicate that the presence of pili, especially Q pili, enhances the attachment of bacteria to bovine cornea in vitro.

PMID: 8095318 [PubMed - indexed for MEDLINE]

Infect. Immun., Dec 1993, 5001-5007, Vol 61, No. 12
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Molecular analysis of the leukotoxin determinants from *Pasteurella haemolytica* serotypes 1 to 16

LL Burrows, E Olah-Winfield and RY Lo

Department of Microbiology, University of Guelph, Ontario, Canada.

All sixteen serotypes of *Pasteurella haemolytica* were shown to produce a leukotoxin protein which is immunologically related to the well- characterized serotype 1 leukotoxin. All of the leukotoxins were weakly hemolytic and were able to bind to BL-3 target cells. The leukotoxin determinants were characterized by Southern blot hybridization by use of the previously cloned serotype 1 determinant as the probe, and a number of distinct classes were identified. The leukotoxin determinants from serotypes 2, 3, and 11 were cloned. Nucleotide sequence analysis of the *lktC* and *lktA* genes of the serotype 3 and 11 determinants revealed nucleotide substitutions throughout the coding sequences. A comparison of the *lktC* and *lktA* genes and deduced proteins of serotypes 1, 3, and 11 showed that they are highly homologous.

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L12: Entry 2 of 15

File: PGPB

Apr 3, 2003

DOCUMENT-IDENTIFIER: US 20030065137 A1

TITLE: Immunological methods to modulate myostatin in vertebrate subjects

CLAIMS:

46. The myostatin multimer of claim 33, wherein said multimer comprises a molecule according to the general formula (MP-X-MP)_y, wherein MP is a myostatin peptide, X is selected from the group consisting of a peptide linkage, an amino acid spacer group, a leukotoxin polypeptide and [MP].sub.n, where n is greater than or equal to 1, and y is greater than or equal to 1.

54. The myostatin immunoconjugate of claim 50, wherein the immunological carrier is a leukotoxin polypeptide.

55. The myostatin immunoconjugate of claim 51, wherein the immunological carrier is a leukotoxin polypeptide.

56. The myostatin immunoconjugate of claim 52, wherein the immunological carrier is a leukotoxin polypeptide.

57. The myostatin immunoconjugate of claim 53, wherein the immunological carrier is a leukotoxin polypeptide.

111. A recombinant vector comprising: (a) a polynucleotide according to claim 104; and (b) control elements that are operably linked to said polynucleotide whereby a coding sequence within said polynucleotide can be transcribed and translated in a host cell, and at least one of said control elements is heterologous to said coding sequence.

112. A recombinant vector comprising: (a) a polynucleotide according to claim 105; and (b) control elements that are operably linked to said polynucleotide whereby a coding sequence within said polynucleotide can be transcribed and translated in a host cell, and at least one of said control elements is heterologous to said coding sequence.

113. A recombinant vector comprising: (a) a polynucleotide according to claim 106; and (b) control elements that are operably linked to said polynucleotide whereby a coding sequence within said polynucleotide can be transcribed and translated in a host cell, and at least one of said control elements is heterologous to said coding sequence.

114. A recombinant vector comprising: (a) a polynucleotide according to claim 107; and (b) control elements that are operably linked to said polynucleotide whereby a coding sequence within said polynucleotide can be transcribed and translated in a host cell, and at least one of said control elements is heterologous to said coding sequence.

115. A recombinant vector comprising: (a) a polynucleotide according to claim 108; and (b) control elements that are operably linked to said polynucleotide whereby a

coding sequence within said polynucleotide can be transcribed and translated in a host cell, and at least one of said control elements is heterologous to said coding sequence.

116. A recombinant vector comprising: (a) a polynucleotide according to claim 109; and (b) control elements that are operably linked to said polynucleotide whereby a coding sequence within said polynucleotide can be transcribed and translated in a host cell, and at least one of said control elements is heterologous to said coding sequence.

117. A recombinant vector comprising: (a) a polynucleotide according to claim 110; and (b) control elements that are operably linked to said polynucleotide whereby a coding sequence within said polynucleotide can be transcribed and translated in a host cell, and at least one of said control elements is heterologous to said coding sequence.

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CLUSTAL FORMAT for T-COFFEE Version_1.37, CPU=0.04 sec, SCORE=22400, Nseq=2, Len=964

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unk|VIRT10457|Blast_submission  -----MSNINVIKSNIQAGLNST-----KSGCLKNLYLAIPKDY
sp|P55118|LKA11_PASHA          MGNKLTNISTNLKSSWLTAKSGLNRTGQSLAKAGQSLKTGAKKIILYIPKDY
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unk|VIRT10457|Blast_submission  TLNDFIKAADELGIARLAEENHTETAKKSVDTVNQFLSLTQTGIAISATKL
sp|P55118|LKA11_PASHA          GLQDLVKAEEELGIEVQKEEGNDIAKAQTSLGTIQNVLGLTERGIVLSAPQL
                                *: *: *: *: *: *      * * . . *: *: *: *: *: *: *: *: *: *

unk|VIRT10457|Blast_submission  TNKLAKGLDSVENIDRKLKASNVLSTLSSFLGTALAGIELDSLIIKKGDAAP
sp|P55118|LKA11_PASHA          -TKVGQAIGSAENLTGFSNAKTVLSGIQSILGSVLGMDLDEALQK-NSNE
                                . *: *: *: *: *: : : *: * * * : *: *: *: *: *: : * : :

unk|VIRT10457|Blast_submission  DLINEIIGNLSQSTQTIEAFSSQLAKLGSTISQAKGFSNIGNKLQNLN-FSK
sp|P55118|LKA11_PASHA          ELTNSLIENIANSVKTLDAFGDQINQLGSKLQNVKGLSSLGDKLKGSLGFDK
                                : * . *: * *: *: *: *: *: *: : * * . : *: *: *: *: *: : . * . *

unk|VIRT10457|Blast_submission  TGLLSGISAGFALADKNASTGKKVAAGFELSNQVIGNVTKAISSYVLAQRVA
sp|P55118|LKA11_PASHA          SGLLSGATAALVLADKNASTSRKVGAGFELANQVVGNIKAVSSYILAQRVA
                                : * * * * : * . . * * * * * * . : * . * * * * . * * . * * . * * . * * * *

unk|VIRT10457|Blast_submission  VAALITSSIMLAISPLAFMNAADKFNHANALDEFKQFRKFGYDGDHLLAEY
sp|P55118|LKA11_PASHA          VAALIASTVSLAISPLAFAGIADKFNHAKSLESYAERFKKLGYDGDNLLAEY
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unk|VIRT10457|Blast_submission  ASLTTISTALGAVSAGVSAAAVGSAVGAPIALLVAGVTGLISGILEASKQAM
sp|P55118|LKA11_PASHA          RSVTAINTALAAIAGGVSAAAGRSVIASPIALLVSGITGVISTILQYSKQAM
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unk|VIRT10457|Blast_submission  QGKILEWEKQNGGQNYFDKGYDSRYAAYLANNLKFLSELNKELEAERVIAIT
sp|P55118|LKA11_PASHA          HNKIVEWEKNNHGKNYFENGYDARYLANLQDNMKFLLNLNKLQEAERVIAIT
                                : . *: . * * * . * * . * * * : * * . * * * : * * * * : * * * * : * * * * *

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sp|P55118|LKA11_PASHA          GDLAGISRLGEKVLSGKAYVDAFEKGHLKADKLVLQDLSANGIIDVSNNGKA
                                *: * * * * : * * * : * * * . * * * : * * : * . . : * * : * * * . * * .

unk|VIRT10457|Blast_submission  SPLLTAGTESRERLTNGKYSYINKLKFGRVKWNQVTDGEASSKLDFSQVIR
sp|P55118|LKA11_PASHA          TPLLTPGTDDRERVQTKGYEYITKLNINRVDSWKITDGAASSTFDLTNNVQR
                                : * * * . * * : * * * . * * . * * : * * . * * . * * : * * : * * : * *

unk|VIRT10457|Blast_submission  -ETEGTDEIGLIVNAKAGNDDIFVGQGKMNIIDGGDGHDRVFYSKDGFGFNIT
sp|P55118|LKA11_PASHA          GNVTKTKETKIVAKLGAGDDNVFVGSQTTEIDGGEGYDRVHYSR-GNYGALT
                                : . * . * : : : * * : * * : * * . : * * * : * * . * * : * . * : *

unk|VIRT10457|Blast_submission  AGSYTVNRKVARGDIYHEVVKRQETKVGKRTETIQYRDYELRKVGYGYQSTD
sp|P55118|LKA11_PASHA          QGSYTVNRFVETGKALHEGTSTHTALVGNREEKIEYR-HSNNQHHAGYYTKD
                                * * * * * * * * . * . * * . : : * * : * . * : * * : . : * * : *

unk|VIRT10457|Blast_submission  IGSQFNDVFKGSKFNDFHSGEGDDLLDGGAGDDRLFGGKGNDRLSGDEGDD
sp|P55118|LKA11_PASHA          IGTSHNDFIKGSKFNDAFNGGDGVDITDGKDGNDRFLFGGKGDDIIDGGNGDD
                                * *: . . *: * * * * * * * * . : . *: * * : * * * : * * * * * : * : . *: *

unk|VIRT10457|Blast_submission  DVLNGGAGNDVYIFRKGDGNDTLYDGTGNDKLAFADANISDIMIERTKEGII
sp|P55118|LKA11_PASHA          DLLHGGKGDDIFVHRQGDGNDIITDSGNDKLSFSDSNLKDLTFEKVKNLNV
                                *: *: * * * : * * : * * * * * : * . * * * * : * : * * : * : * . : :

unk|VIRT10457|Blast_submission  SINIPRWY----ITSNLQNYQSNKTDHKIEQLIGKDGSYITSQDQIDKILQDK
sp|P55118|LKA11_PASHA          KVTIQDWFREADFKEVRNYKATK-DEKIEEIIGQNGERITSKQVDDLI--A

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...* *:*:..* *.***:***:*. ***.*:*.:

unk|VIRT10457|Blast_submission QELKKLADENKSQKLSASDIASSLNKLVGSMALFGTANSVSSNALQPITQPT
 sp|P55118|LKA11_PASHA DELSKVVDNYELLKHS-KNVTNSLDKLISSASAFTSSNDSRNVLVAPTSMLD
 :***.*:.*: : * **:***:*. * : * :*. . : * :

unk|VIRT10457|Blast_submission ----
 sp|P55118|LKA11_PASHA ARAA